activity to desensitize the dentin, and such actives are thus incorporated in oral care products for protection of sensitive teeth. Indeed the disclosure at page 27, lines 17-18 has defined what is meant by the phrase by reciting examples of known dentinal desensitizing agents, i.e., strontium chloride, potassium nitrate, stannous fluoride and sodium fluoride.

With regard to the phrase "whole body health", Applicants refer the Examiner to the definition at page 7, lines 23-27 as follows:

> By "whole body health" as used herein is meant overall systemic health characterized by a reduction in risk of development of major systemic diseases and conditions including cardiovascular disease, stroke, diabetes, severe respiratory infections, premature births and low birth weights (including post-partum dysfunction in neurologic/developmental function), and associated increased risk of mortality.

The present invention as now claimed is specific to a method for promoting whole body health or systemic health. The method involves topically administering a composition comprising a host response modulating agent, specifically a H2 antagonist, to the oral cavity as opposed to systemic administration. The present claims are based on Applicants' discovery of a new use for a method of treatment of the oral cavity. Specifically Applicants have discovered that topical administration to the oral cavity of compositions comprising a host response modulating agent is beneficial in promoting systemic health in addition to treating or preventing bacteria-mediated oral cavity conditions. In particular, the present method effectively decreases etiologic factors that contribute to development of certain systemic diseases such as heart disease. By decreasing the etiologic factors for a systemic disease, the risk of developing such a disease is also decreased leading to better overall health for the subject.

Claims Rejection Under 35 USC § 102(b)

Claims 1-4 and 7 have been rejected under 35 USC § 102(b) as being anticipated by Pan et al. (WO 97/16159) and by commonly assigned Singer et al. (US 5,364,616). Claims 1-2 are rejected under 35 USC § 102(b) as anticipated by Tsujita et al. (JP 04/089428). The Examiner contends that the whole body health benefits are inherent in the referenced methods.

Applicants respectfully traverse the Examiner's rejection of the claims in view of each of the references as each would apply to the claims as amended herein. Claims 1, 5 and 6 are withdrawn from consideration at this time.

The present claims define a method for promoting whole body health by topical administration to the oral cavity of a composition comprising a H2 antagonist. The present method promotes whole body health (or overall systemic health) by effectively modulating the body's response to pathogenic oral bacteria, associated bacterial toxins and endotoxins, and inflammatory mediators and cytokines prompted by these pathogenic bacteria, all believed to be involved in the etiology of certain systemic diseases including cardiovascular disease, stroke, diabetes, severe respiratory infections, premature births and low birth weights (including post-partum dysfunction in neurologic/developmental function). By reducing these etiologic or causative factors, the risk of development of these systemic diseases is likewise reduced, leading to better whole body health.

For example, it has been known that bacteria may affect the heart and other organs of the body. Now evidence is mounting that suggests people with periodontitis, a bacteria-mediated disease of the oral cavity, may

be more at risk for heart disease, and have a significantly higher risk of having a fatal heart attack than patients without periodontitis. One theory to explain the link between periodontal disease and heart disease is that oral pathogenic bacteria enter the blood through inflamed gums, attach to fatty plaques in the coronary arteries (heart blood vessels) and cause small blood clots that contribute to clogged arteries. It has been reported that 70% of the fatty plaque that blocks carotid arteries and causes stroke contain bacteria. Forty percent of those bacteria have been traced to the mouth. Coronary artery disease is characterized by a thickening of the walls of the coronary arteries due to the buildup of fatty proteins. Blood clots can obstruct normal blood flow, restricting the amount of nutrients and oxygen required for the heart to function properly. This may lead to heart attacks. Another possibility is that changes in systemic inflammatory mediators caused by periodontitis increase development of atherosclerotic plaque, which then contributes to thickening of the arterial walls.

By the present claimed method, spread into the bloodstream and other parts of the body of pathogenic bacteria and associated harmful substances including toxins and endotoxins is prevented or minimized. The result is a decrease in the causative factors for certain diseases and a corresponding decrease in the risk of development of these systemic diseases, such as heart disease. Thus, the present claims are directed to a new use for a method that traditionally has been used solely for locally treating or preventing bacteria-mediated diseases and conditions of the oral cavity.

The Examiner's attention is further directed to the attached declaration by present inventor Robert E. Singer, Jr., presenting findings relevant to the mechanism of action of topical H2 antagonists. The present claims are based on the discovery that topical treatment of the oral tissues with H2 antagonists serves to increase the gingival barrier function of the periodontal tissues. From a series of studies conducted under Mr. Singer's direction, it has been demonstrated that topical H2 antagonists (1) increase gingival crevicular polymorphonuclear (PMN) function for the phagocytosis and killing of bacterial pathogens; (2) elevate the levels of gingival crevicular antibodies during experimental periodontitis; and (3) increase the levels of gingival crevicular fluid (GCF) IgA, a marker for the protective gingival tissue response. Taken together, these findings indicate that H2 antagonists enhance the function of key mechanisms of the gingival barrier function.

From these new findings, it is evident that the topical application of H2 antagonists to oral tissues represents a unique and unanticipated approach to increasing the barrier function of periodontal tissues. The abililty of H2 antagonists to increase the natural barrier function of gingival tissues is an extremely important benefit in as much as this unique mechanism of action enables providing not only a benefit vs. periodontal disease but unexpectedly also represents an effective approach to preventing oral pathogens and their products from entering into either the gingival tissues or the systemic circulation. Consequently, topical application of H2 antagonists affords unanticipated benefits for preventing oral pathogens from prompting the systemic inflammatory mechanisms and complications that contribute to systemic diseases/disorders such as atherosclerosis, stroke, diabetes, and low birth weight infants.

Applicants respectfully submit that the present method claims directed to a new use of topical administration of a H2 antagonist are novel and unobvious in view of the cited references. There is no disclosure nor any suggestion in any one of Pan et al. (WO 97/16159), Singer et al. (US 5,364,616), or Tsujita et al. (JP 04/089428) with regard to whole body health or systemic health, much less that the present H2 antagonist containing compositions administered topically to the oral cavity would promote whole body health by decreasing causative or risk factors leading to the development of certain systemic diseases.

Applicants also traverse the Examiner's contention that the present method claims are not patentable because the results of the claimed methods, i.e., "whole body health benefits", are inherent. The present method claims fall within the definition under 35 USC. § 100(b) for a patentable "process" (under § 101) which means process, art or method, and includes a ***new use of a known process, machine, manufacture, composition or matter or material*** (emphasis added). Thus, "a process or method which involves only a new use of an old material is patentable." *Howes v. Great Lakes Press Corp.*, 679 F.2d 1023, 1029 (2d Cir.), which found that Howes' claim to a method which makes possible the faithful transfer of color art work to fabric by means of treated heat transfer paper was patentable because Howes created a *new use of a known process*. Similarly, *claims drawn to a method for using either an old or "obvious" composition, wherein the method has unobvious beneficial or useful effects, have been found patentable even though the composition itself could not be patented.* [*In re Shetty*, 566 F.2d 81, 83, 195 USPQ 753, 754 (CCPA 1977); *In re Legator*, 53 CCPA, 729, 352 F.2d 377 (1965); *Joseph Bancroft & Sons Co. v. Watson*, 170 F. Supp. 78 (D.D.C. 1959), 120 USPQ 265].

Clearly, the issue relevant to the patentability of the present method is whether or not the claimed new use is obvious to one of skill in the art. Applicants submit that the present claimed methods have unobvious beneficial and useful effects of promoting whole body health. That this benefit might be inherent "is quite immaterial if, as the record establishes here, one of ordinary skill in the art would not appreciate or recognize that inherent result." [*In re Floyd E. Naylor*, 54 CCPA 902, 369 F.2d 765 (1966), 152 USPQ 106; *In re Shetty*, 566 F.2d 81, 83, 195 USPQ 753, 754 (CCPA 1977].

CONCLUSION

Applicants respectfully request reconsideration of this application, entry of the amendments, withdrawal of the 35 USC §112, first paragraph rejection, withdrawal of the claims rejections under §102(b) and allowance of all application claims.

Attached hereto is a marked-up version of the changes made to claims by the current amendments. The attached page is captioned "**Version With Markings to Show Changes Made**".

Respectfully submitted,

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Version With Markings to Show Changes Made

Claims 1, 5 and 6 are canceled without prejudice.

Claims 2, 3, 4 and 7 are amended as follows.

2. (Twice Amended) A method for [treating and preventing oral cavity diseases in human and other animal subjects and thereby] promoting whole body health in [said] human and other animal subjects, comprising topically administering to said subjects' oral cavity, a composition [according to Claim 1] comprising a safe and effective amount of a host-response modulating agent and a pharmaceutically acceptable oral carrier, wherein said host-response modulating agent is a H2-antagonist.

3. (Twice Amended) A method for [treating and preventing oral cavity diseases in human and other animal subjects and thereby] promoting whole body health in [said] human and other animal subjects according to Claim 2, wherein said composition is in a form selected from the group consisting of a mouthrinse, toothpaste, tooth gel, tooth powder, non-abrasive gel, chewing gum, mouth spray, lozenge, dental implement, and a pet care product.

4. (Twice Amended) A method for [treating and preventing oral cavity diseases in human and other animal subjects and thereby] promoting whole body health in [said] human and other animal subjects according to Claim 2, wherein said host-response modulating agent is a H-2 antagonist selected from the group consisting of cimetidine, etintidine, ranitidine, ICIA-5165, tiotidine, ORF-17578, lupitidine, donetidine, famotidine, roxatidine, pifatidine, lamtidine, BL-6548, BMY-25271, zaltidine, nizatidine, mifentidine, BMY-25368 (SKF-94482), BL-6341A, ICI-162846, ramixotidine, Wy-45727, SR-58042, BMY-25405, loxtidine, DA-4634, bisfentidine, sufotidine, ebrotidine, HE-30-256, D-16637, FRG-8813, FRG-8701, impromidine, L-643728, HB-408, and mixtures thereof.

7. (Twice Amended) A method for [treating and preventing oral cavity diseases in human and other animal subjects and thereby] promoting whole body health in [said] human and other animal subjects according to Claim 2, wherein said composition topically administered to said subjects comprises an additional therapeutic active selected from the group consisting of antimicrobial/antiplaque agents, biofilm inhibiting agents, antibiotics; analgesics and local anesthetic agents; dentinal desensitizing agents; odor masking agents; and mixtures thereof.